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# EXPERIMENTS

TO DETERMINE

THE INFLUENCE OF DIGITALIS ON NORMAL TEMPERATURES

AND

ITS ACTION AS AN ANTIPYRETIC IN TYPHOID FEVER.

BY

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## THE INFLUENCE OF DIGITALIS ON NORMAL TEMPERATURES

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THAT toxic doses of digitalis lower the temperature in healthy men and animals, and that this fall is preceded by a temporary rise, has been proven experimentally by numerous observers. From the present state of our knowledge these phenomena appear without doubt to be due to changes in the circulation. Clinical data, however, have been wanting as to the action of therapeutic doses in health and disease. The following results obtained from the administration of this drug in a series of cases in the medical wards of the University Hospital are of interest and importance :

I. The first series of cases are recorded for the purpose of showing the action of therapeutic doses upon normal temperatures. In seventeen cases of organic heart-disease with normal temperature the administration of digitalis was followed by a subnormal temperature, ranging from  $96.3^{\circ}$  to  $97.8^{\circ}$  throughout its use.

Upon admission the above cases were placed under the most perfect hygienic con-

ditions. Absolute rest, bed-pan imperative, and perfect quiet insisted upon. No drug was administered directly to the heart, and careful attention was given to diet.

In all the cases so treated the pulse, respiration, and temperature soon fell to normal. In most cases any slight rise upon admission was usually referable to the excitement attendant upon access to the hospital ward. In the majority of cases this mode of treatment sufficed. The temperature, pulse, and respiration were then noted at regular intervals. Those cases which showed a normal range continuously for several days were selected. From the sixth to tenth day after admission the drug was administered either in the form of the tincture or infusion. The temperature, pulse, and respiration were then registered every one or two hours throughout its use.

Of seventeen selected cases in no instance could a rise in the temperature be detected.

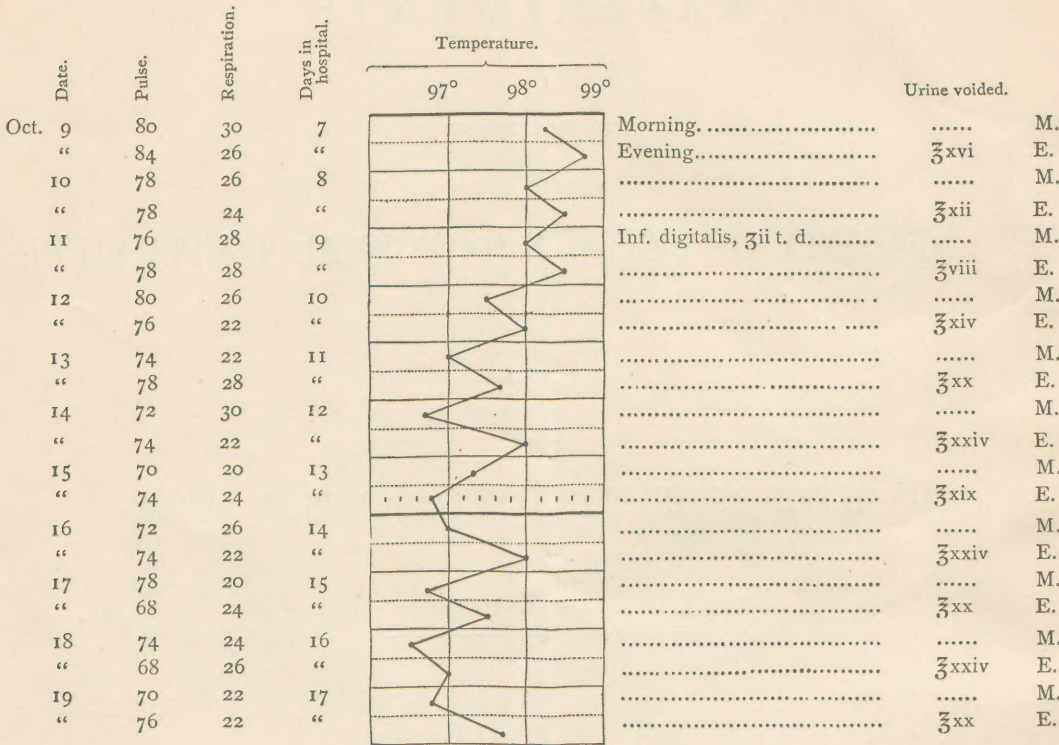
In all the cases, after the administration of digitalis, the temperatures became subnormal,

ranging between 96.2° and 97.8°, and remained so from one to two days after we ceased its administration.

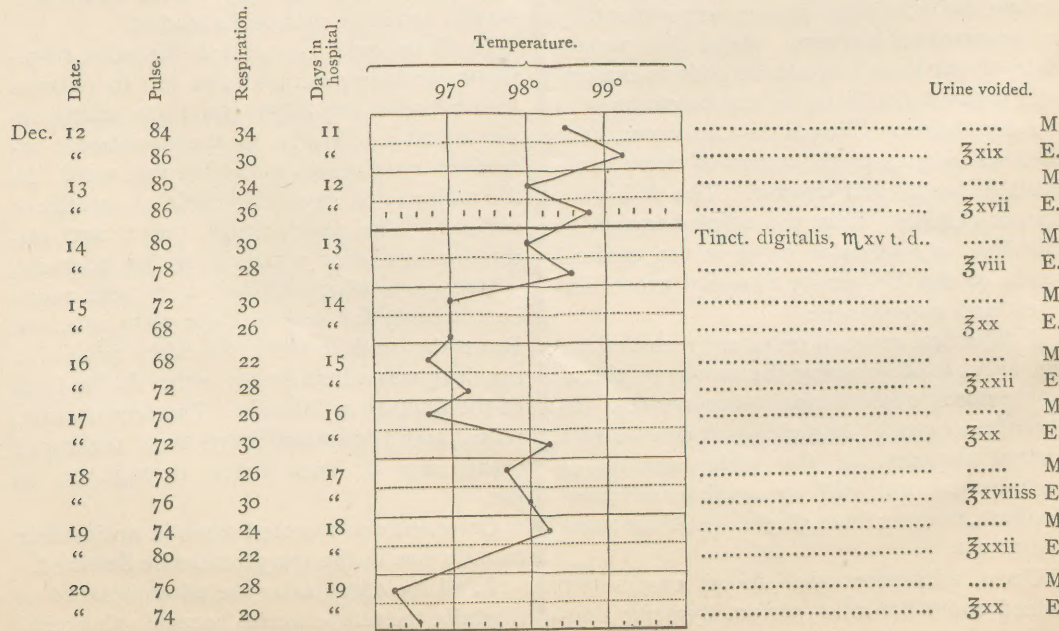
The following charts show its effect upon the heart, respiration, and normal tempera-

ture in two of the cases under observation. In the first case, the infusion was used ; in the second, the tincture. Want of space prevents further reference. These appended, however, are types of the remaining charts.

CASE I.—L. G.



CASE II.—M. L.





II. The second series of cases are appended for the purpose of showing the action of therapeutic doses of digitalis upon the pulse, respiration, and temperature in fever.

The following temperature charts are selected from ten (10) cases of typhoid, showing its action upon the pulse, respiration, and temperature curve.

CASE I.—J. M.

Date.	Pulse.	Respiration.	Days in hospital.	Temperature.		
				99°	100°	101°
...	94	24	11			
...	96	28	"			
...	...	...	"			
...	...	...	"			
...	102	28	"			
...	110	28	12			
...	100	26	"			
...	98	26	"			
...	...	...	"			
...	92	24	"			
...	...	...	"			
...	...	...	"			
...	90	24	"			
...	...	...	"			
...	...	...	"			
...	...	...	"			
...	...	...	13			
...	...	...	"			

.....	4 P.M.
.....	6 "
.....	8 "
.....	10 "
.....	12 midnight.
.....	Digitalis, m̄xv. 2 A.M.
.....	4 "
.....	6 "
.....	Digitalis, m̄xv. 8 "
.....	10 "
.....	12 "
.....	Digitalis, m̄xv. 2 P.M.
.....	4 "
.....	6 "
.....	8 "
.....	10 "
.....	12 midnight.
.....	2 A.M.
.....	4 "

CASE II.—C. P.

Date.	Pulse.	Respiration.	Days in hospital.	Temperature.	
...	...	...	18	99°	10 P.M.
...	...	...	"		12 midnight.
...	...	...	19		2 A.M.
...	100	32	"		Digitalis, $\mathfrak{m}$ xv..... 4 "
...	100	32	"		6 "
...	96	30	"		8 "
...	...	...	"		Digitalis, $\mathfrak{m}$ xv..... 10 "
...	90	26	"		12 "
...	...	...	"		2 P.M.
...	...	...	"		Digitalis, $\mathfrak{m}$ xv..... 4 "
...	90	24	"		6 "
...	...	...	"		8 "
...	94	24	"		10 "
...	...	...	"		12 midnight.
...	...	...	"		2 A.M.
...	...	...	20		4 "
...	...	...	"		6 "
...	...	...	"		8 "



In six cases there was noted, besides a fall in the pulse and respiration, a decided fall in the temperature.

In three cases there was but a slight fall in the temperature.

In one case no fall in the temperature was to be noted.

In nine cases the temperature fell from 1.5° to 3° Fahr., and remained low throughout the course of the disease.

The treatment of the above cases was expectant in character,—rest, careful attention to diet, and alcohol. The heart was watched, and it was when the alcohol appeared to lose its effect, when the nervous system had lost all control of this organ, when the pulse was weak, rapid, dicrotic, small, and often intermittent, that digitalis proved itself the most powerful remedy we had resort to to meet this indication, and offered the most promising results; the pulse became slower, the respirations calmer, the delirium often ceased, and the whole condition of the patient changed. Hyperpyrexia was treated principally by sponging, and it was in just such cases where we had that condition described as a “delirium of temperature,” where the temperature oscillated with the application and withdrawal of cold, that digitalis proved its permanent antipyretic action, which was stimulating rather than depressing in character.

In the above cases the drug was used *primarily* for its action upon the heart, and *secondarily* for its antipyretic action.

A careful review of the literature of the subject discloses the fact that the use of digitalis for its antipyretic effect is not new, though the literature is meagre; with the exception of Wunderlich's article (“Upon Typhoid Fever,” *Manual of Medical Thermometry*, *Syd. Soc. Trans.*) clinical observation is conspicuous by its absence.

Wunderlich's conclusions were criticised (Wood), as the drug was administered during the third and fourth weeks of the fever, at a period when natural defervescence was likely to take place.

In the cases recorded since the drug was given at varying periods during the course of the disease; the pulse and temperature being our guide, the possibility of such an error must be excluded, as in the majority of cases it was given for rising temperatures, and frequently, when the administration was stopped for any time, the temperature showed a tendency to rise.

Wunderlich (*Arch. der Heilk.*, 1862) deserves the credit of having first introduced

the use of digitalis as an antipyretic in typhoid fever.

Soon after the appearance of Wunderlich's article, digitalis was used upon the Continent, but had few followers in England (Phillips).

Liebermeister (“Ziemssen's Encyclop.,” vol. iii.) has used it with asserted good results in combination with the cold-water treatment.

Hankel (*Arch. der Heilk.*, 1869) gives results from its use as an antipyretic in an epidemic of typhoid fever. Though worthy of notice, he found his mortality was not diminished (twelve per cent.).

Ringer (“Handb. of Therap.”) found that digitalis reduces temperature, but that large doses were required.

Lauder-Brunton found it useless.

Trousseau (vol. iii.) claims that the antipyretic action of digitalis has not equalled in practice its therapeutic promises.

With the idea that digitalis is an active antipyretic, it has been prescribed in various acute diseases with asserted good results. To use it entirely for this purpose we are justified in agreeing with those observers who assert that the field for digitalis is not fever. The result of these investigations lead us to conclude that the great indications for digitalis in typhoid fever are,—first, a weak heart, for its stimulating action, and hyperpyrexia, associated with a weak heart, for its antipyretic action, and that a strong, full pulse is a contraindication to its use, even though it be associated with a high temperature.

It has been held that digitalis is only to be used in those cases in which there is no considerable degree of cardiac weakness, when the pulse is not yet extremely frequent, or at least pretty strong.

Liebermeister holds that the rule for its application in fever is just the opposite to what it is in diseases of the heart; in other words, that the more frequent the pulse the less is digitalis indicated.

The view that the impending paralysis of the heart is not prevented by the use of this drug, but rather favored thereby, must be at least tentative.

It has been proven experimentally that as the blood-pressure rises the temperature falls, under the action of this drug; clinical observations corroborate this statement, and there can be no doubt that such is the antipyretic action of digitalis. This assertion is in accord with the experiments of Heidenhain, who found that a rise in the blood-pressure invariably produced a fall in the tempera-



ture. That the antipyretic action of digitalis is produced through changes in the circulation there can be no doubt.

From the above clinical observations it may be said that, therapeutically,—

I. *Digitalis* depresses normal temperatures from one to one and a half degrees; that this subnormal range remains from one to two days after the administration has ceased.

*In typhoid fever* it may be said,—

I. *Digitalis* reduces the pulse-rate, diminishes the respirations, and depresses the temperature.

II. That with a fall in the pulse and respirations there is a corresponding decline in the temperature.

III. That a weak heart is no contraindication to its use.

IV. The main indication for its use is a weak heart, independent of hyperpyrexia.

V. Though a most powerful antipyretic in treatment of hyperpyrexia when associated with a weak heart, it should not, however, be used to meet this indication when there are no evidences of cardiac weakness,—*i.e.*, when the pulse is strong, full, and bounding.

*Administration.*—Both the tincture and infusion were used, preferably the tincture in typhoid fever and infusion in chronic heart-disease. We found no hesitation in using the tincture hypodermically in typhoid fever when the stomach refused to retain it. It has been used since the above cases were treated, in combination with quinine, and in addition to the cold-water treatment, with good results.

In conclusion, the writer wishes to express his heartfelt thanks to Dr. William Pepper and Dr. William Osler for reference to the cases treated in their wards.









